

# MAR 0 1 2004 CIBT-P01-130SequenceListing

| MAR U LOU ELISTING  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---|----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| <110> Huston, J.  Houston, L.L. Ring, D. Oppermann, H.  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| BIOSYNTHETIC BINDING PROTEINS FOR IMMUNO-TARGETING  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| CIBT-P01-130  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 09/558,741<br>2000-04-26  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 07/831,967<br>1992-02-06  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <160> 16  | 16 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :170> PatentIn version 3.1  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <210> 1<br><211> 909<br><212> DNA<br><213> Artificial Sequence  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <220> <223> 741F8 sFv'  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <220> <221> CDS <222> (3)(752) <223>  |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <pre>&lt;400&gt; 1 cc atg gcg gag atc caa ttg gtg cag tct gga cct gag ctg aag aag    Met Ala Glu Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys    1</pre> |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| cct gga gag aca gtc aag atc tcc tgc aag gct tct ggg tat acc ttc Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe 20 25 30                    | 95 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| aca aac tat gga atg aac tgg gtg aag cag gct cca gga aag ggt tta 14<br>Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu<br>35 40 45           | 43 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| aag tgg atg ggc tgg ata aac acc aac act gga gag cca aca tat gct 19 Lys Trp Met Gly Trp Ile Asn Thr Asn Thr Gly Glu Pro Thr Tyr Ala 50 55 60                 | 91 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| gaa gag ttc aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc Glu Glu Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser 65 70 75                    | 39 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| act gcc tat ttg cag atc aag aag ctc aaa aat gag gac acg gct aca Thr Ala Tyr Leu Gln Ile Lys Lys Leu Lys Asn Glu Asp Thr Ala Thr 80 85 90 95                 | 87 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| tat ttc tgt gga agg caa ttt att acc tac ggc ggg ttt gct aac tgg 33<br>Page 1  | 35 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

| Tyr                          | Phe               | Cys                      | Gly               | Arg<br>100        | Gln               | Phe               | IJE               | Thr               | Tyr<br>105        | useq<br>Gly       | uenc<br>Gly       | eL1s<br>Phe       | ting<br>Ala       | Asn<br>110        | Trp               |     |
|------------------------------|-------------------|--------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| ggc<br>Gly                   | caa<br>Gln        | ggg<br>Gly               | act<br>Thr<br>115 | ctg<br>Leu        | gtc<br>Val        | act<br>Thr        | gtc<br>Val        | tct<br>Ser<br>120 | gca<br>Ala        | tcg<br>Ser        | agc<br>Ser        | tcc<br>Ser        | tcc<br>Ser<br>125 | gga<br>Gly        | tct<br>Ser        | 383 |
| tca<br>Ser                   | tct<br>Ser        | agc<br>Ser<br>130        | ggt<br>Gly        | tcc<br>Ser        | agc<br>Ser        | tcg<br>Ser        | agc<br>Ser<br>135 | gat<br>Asp        | atc<br>Ile        | gtc<br>Val        | atg<br>Met        | acc<br>Thr<br>140 | cag<br>Gln        | tct<br>Ser        | cct<br>Pro        | 431 |
| aaa<br>Lys                   | ttc<br>Phe<br>145 | atg<br>Met               | tcc<br>Ser        | acg<br>Thr        | tca<br>Ser        | gtg<br>Val<br>150 | gga<br>Gly        | gac<br>Asp        | agg<br>Arg        | gtc<br>Val        | agc<br>Ser<br>155 | atc<br>Ile        | tcc<br>Ser        | tgc<br>Cys        | aag<br>Lys        | 479 |
| gcc<br>Ala<br>160            | agt<br>Ser        | cag<br>Gln               | gat<br>Asp        | gtg<br>Val        | agt<br>Ser<br>165 | act<br>Thr        | gct<br>Ala        | gta<br>Val        | gcc<br>Ala        | tgg<br>Trp<br>170 | tat<br>Tyr        | caa<br>Gln        | caa<br>Gln        | aaa<br>Lys        | cca<br>Pro<br>175 | 527 |
| ggg<br>Gly                   | caa<br>Gln        | tct<br>Ser               | cct<br>Pro        | aaa<br>Lys<br>180 | cta<br>Leu        | ctg<br>Leu        | att<br>Ile        | tac<br>Tyr        | tgg<br>Trp<br>185 | aca<br>Thr        | tcc<br>Ser        | acc<br>Thr        | cgg<br>Arg        | cac<br>His<br>190 | act<br>Thr        | 575 |
| gga<br>Gly                   | gtc<br>Val        | cct<br>Pro               | gat<br>Asp<br>195 | cgc<br>Arg        | ttc<br>Phe        | aca<br>Thr        | ggc<br>Gly        | agt<br>Ser<br>200 | gga<br>Gly        | tct<br>Ser        | ggg<br>Gly        | aca<br>Thr        | gat<br>Asp<br>205 | tat<br>Tyr        | act<br>Thr        | 623 |
| ctc<br>Leu                   | acc<br>Thr        | atc<br>Ile<br>210        | agc<br>Ser        | agt<br>Ser        | gtg<br>Val        | cag<br>Gln        | gct<br>Ala<br>215 | gaa<br>Glu        | gac<br>Asp        | ctg<br>Leu        | gca<br>Ala        | ctt<br>Leu<br>220 | cat<br>His        | tac<br>Tyr        | tgt<br>Cys        | 671 |
| cag<br>Gln                   | caa<br>Gln<br>225 | cat<br>His               | tat<br>Tyr        | aga<br>Arg        | gtg<br>Val        | ccg<br>Pro<br>230 | tac<br>Tyr        | acg<br>Thr        | ttc<br>Phe        | gga<br>Gly        | ggg<br>Gly<br>235 | ggg<br>Gly        | acc<br>Thr        | aag<br>Lys        | ctg<br>Leu        | 719 |
| gag<br>Glu<br>240            | ata<br>Ile        | aaa<br>Lys               | cgg<br>Arg        | gct<br>Ala        | gat<br>Asp<br>245 | ggg<br>Gly        | gga<br>Gly        | ggt<br>Gly        | gga<br>Gly        | tgt<br>Cys<br>250 | taac              | gggg              | gga g             | gtgg              | gatgtt            | 772 |
| gggt                         | ctcg              | jtt a                    | cgtt              | gcgg              | ja to             | tcga              | iggct             | ato               | ttta              | ıcta              | acto              | ttac              | cg t              | aaag              | gttctg            | 832 |
| gcto                         | aact              | gt d                     | tgca              | ecgca             | a go              | tttt              | gcag              | g gat             | atca              | itga              | gcgc              | ttaa              | aga t             | ccgt              | tcgacc            | 892 |
| tgca                         | aggca             | itg c                    | aago              | tt                |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 909 |
| <210<br><211<br><212<br><213 | l> 2<br>2> F      | 2<br>250<br>PRT<br>Artif | -<br>icia         | al Se             | equer             | ıce               |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
| <220<br><223                 |                   | 741F8                    | } sF∖             | <b>,'</b>         |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
| <400                         |                   |                          |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |
| Met<br>1                     | Ala               | Glu                      | Ile               | Gln<br>5          | Leu               | ۷al               | Gln               | Ser               | Gly<br>10         | Pro               | Glu               | Leu               | Lys               | Lys<br>15         | Pro               |     |

Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr 20 25 30 Page 2

Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys 35 40 45

Trp Met Gly Trp Ile Asn Thr Asn Thr Gly Glu Pro Thr Tyr Ala Glu 50 60

Glu Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr 65 70 75 80

Ala Tyr Leu Gln Ile Lys Lys Leu Lys Asn Glu Asp Thr Ala Thr Tyr 85 90 95

Phe Cys Gly Arg Gln Phe Ile Thr Tyr Gly Gly Phe Ala Asn Trp Gly 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ala Ser Ser Ser Ser Gly Ser Ser 115 120 125

Ser Ser Gly Ser Ser Ser Ser Asp Ile Val Met Thr Gln Ser Pro Lys 130 135 140

Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Ser Cys Lys Ala 145 150 155 160

Ser Gln Asp Val Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ser Pro Lys Leu Leu Ile Tyr Trp Thr Ser Thr Arg His Thr Gly 180 185 190

Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu 195 200 205

Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Leu His Tyr Cys Gln 210 220

Gln His Tyr Arg Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu 225 230 235 240

Ile Lys Arg Ala Asp Gly Gly Gly Cys 245 250

<210> 3

<211> 779

<212> DNA

<213> Artificial Sequence

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|-------------------|---|---|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| <22               | 221> CDS<br>222> (3)(758)<br>223>   |   |                   |                   |                   |                   |                   |                   |                   |                    |                   |                   |                   |                   |                   |     |
| CC                | <pre>&lt;400&gt; 3 cc atg gaa gtt caa ctg caa cag tct ggt cct gaa ttg gtt aaa cct    Met Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro    1</pre> |   |                   |                   |                   |                   |                   |                   |                   |                    |                   |                   |                   |                   |                   | 47  |
| ggc<br>Gly        | gcc<br>Ala  | tct<br>Ser                              | gtg<br>Val        | cgc<br>Arg<br>20  | atg<br>Met        | tcc<br>Ser        | tgc<br>Cys        | aaa<br>Lys        | tcc<br>Ser<br>25  | tct<br>Ser         | ggg<br>Gly        | tac<br>Tyr        | att<br>Ile        | ttc<br>Phe<br>30  | acc<br>Thr        | 95  |
| gac<br>Asp        | ttc<br>Phe  | tac<br>Tyr                              | atg<br>Met<br>35  | aat<br>Asn        | tgg<br>Trp        | gtt<br>Val        | cgc<br>Arg        | cag<br>Gln<br>40  | tct<br>Ser        | cat<br>His         | ggt<br>Gly        | aag<br>Lys        | tct<br>Ser<br>45  | cta<br>Leu        | gac<br>Asp        | 143 |
| tac<br>Tyr        | atc<br>Ile  | ggg<br>Gly<br>50                        | tac<br>Tyr        | att<br>Ile        | tcc<br>Ser        | cca<br>Pro        | tac<br>Tyr<br>55  | tct<br>Ser        | ggg<br>Gly        | gtt<br>Val         | acc<br>Thr        | ggc<br>Gly<br>60  | tac<br>Tyr        | aac<br>Asn        | cag<br>Gln        | 191 |
| aag<br>Lys        | ttt<br>Phe<br>65  | aaa<br>Lys                              | ggt<br>Gly        | aag<br>Lys        | gcg<br>Ala        | acc<br>Thr<br>70  | ctt<br>Leu        | act<br>Thr        | gtc<br>Val        | gac<br>Asp         | aaa<br>Lys<br>75  | tct<br>Ser        | tcc<br>Ser        | tca<br>Ser        | act<br>Thr        | 239 |
| gct<br>Ala<br>80  | tac<br>Tyr  | atg<br>Met                              | gag<br>Glu        | ctg<br>Leu        | cgt<br>Arg<br>85  | tct<br>Ser        | ttg<br>Leu        | acc<br>Thr        | tct<br>Ser        | gag<br>Glu<br>90   | gac<br>Asp        | tcc<br>Ser        | gcg<br>Ala        | gta<br>Val        | tac<br>Tyr<br>95  | 287 |
| tat<br>Tyr        | tgc<br>Cys  | gcg<br>Ala                              | ggc<br>Gly        | tcc<br>Ser<br>100 | tct<br>Ser        | ggt<br>Gly        | aac<br>Asn        | aaa<br>Lys        | tgg<br>Trp<br>105 | gcc<br>Ala         | atg<br>Met        | gat<br>Asp        | tat<br>Tyr        | tgg<br>Trp<br>110 | ggt<br>Gly        | 335 |
| cat<br>His        | ggt<br>Gly  | gct<br>Ala                              | agc<br>Ser<br>115 | gtt<br>Val        | act<br>Thr        | gtg<br>Val        | agc<br>Ser        | tcc<br>Ser<br>120 | tcc<br>Ser        | gga<br>Gly         | tct<br>Ser        | tca<br>Ser        | tct<br>Ser<br>125 | agc<br>Ser        | ggt<br>Gly        | 383 |
| tcc<br>Ser        | agc<br>Ser  | tcg<br>Ser<br>130                       | agt<br>Ser        | gga<br>Gly        | tcc<br>Ser        | gac<br>Asp        | gtc<br>Val<br>135 | gta<br>Val        | atg<br>Met        | acc<br>Thr         | cag<br>Gln        | act<br>Thr<br>140 | ccg<br>Pro        | ctg<br>Leu        | tct<br>Ser        | 431 |
| ctg<br>Leu        | ccg<br>Pro<br>145   | gtt<br>Val                              | tct<br>Ser        | ctg<br>Leu        | ggt<br>Gly        | gac<br>Asp<br>150 | cag<br>Gln        | gct<br>Ala        | tct<br>Ser        | att<br>Ile         | tct<br>Ser<br>155 | tgc<br>Cys        | cgc<br>Arg        | tct<br>Ser        | tcc<br>Ser        | 479 |
| cag<br>Gln<br>160 | tct<br>Ser  | ctg<br>Leu                              | gtc<br>Val        | cat<br>His        | tct<br>Ser<br>165 | aat<br>Asn        | ggt<br>Gly        | aac<br>Asn        | act<br>Thr        | tac<br>Tyr<br>170  | ctg<br>Leu        | aac<br>Asn        | tgg<br>Trp        | tac<br>Tyr        | ctg<br>Leu<br>175 | 527 |
| caa<br>Gln        | aag<br>Lys  | gct<br>Ala                              | ggt<br>Gly        | cag<br>Gln<br>180 | tct<br>Ser        | ccg<br>Pro        | aag<br>Lys        | ctt<br>Leu        | ctg<br>Leu<br>185 | atc<br>Ile         | tac<br>Tyr        | aaa<br>Lys        | gtc<br>Val        | tct<br>Ser<br>190 | aac<br>Asn        | 575 |
| cgc<br>Arg        | ttc<br>Phe  | tct<br>Ser                              | ggt<br>Gly<br>195 | gtc<br>Val        | ccg<br>Pro        | gat<br>Asp        | cgt<br>Arg        | ttc<br>Phe<br>200 | tct<br>Ser        | ggt<br>Gly         | tct<br>Ser        | ggt<br>Gly        | tct<br>Ser<br>205 | ggt<br>Gly        | act<br>Thr        | 623 |
| gac<br>Asp        | ttc<br>Phe  | acc<br>Thr                              | ctg<br>Leu        | aag<br>Lys        | atc<br>Ile        | tct<br>Ser        | cgt<br>Arg        | gtc<br>Val        | GIn               | gcc<br>Ala<br>Page | Glu               | gac<br>Asp        | ctg<br>Leu        | ggt<br>Gly        | atc<br>Ile        | 671 |

719

768

779

210

tac ttc tgc tct cag act act cat gta ccg ccg act ttt ggt ggc Tyr Phe Cys Ser Gln Thr Thr His Val Pro Pro Thr Phe Gly Gly Gly 230 acc aag ctc gag att aaa cgt tcc ggg gga ggt gga tgt taactgcagc Thr Lys Leu Glu Ile Lys Arg Ser Gly Gly Gly Cys 240 245 250 ccgggggatc c <210> <211> 252 <212> PRT Artificial Sequence <220> <223> 26-10 sFv' <400> Met Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly 10 15 Ala Ser Val Arg Met Ser Cys Lys Ser Ser Gly Tyr Ile Phe Thr Asp 20 25 30 Phe Tyr Met Asn Trp Val Arg Gln Ser His Gly Lys Ser Leu Asp Tyr 35 40 45 Ile Gly Tyr Ile Ser Pro Tyr Ser Gly Val Thr Gly Tyr Asn Gln Lys 50 60 Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala 65 70 75 80 Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr 85 90 95 Cys Ala Gly Ser Ser Gly Asn Lys Trp Ala Met Asp Tyr Trp Gly His 100 105 110 Gly Ala Ser Val Thr Val Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln 145 150 155 160

|                                      |  | _                | _                |                 |                  | _                | CIB              | T-P0             | 1-13             | 0seq               | uenc             | eLis             | ting             |                  |                  |     |
|--------------------------------------|--|------------------|------------------|-----------------|------------------|------------------|------------------|------------------|------------------|--------------------|------------------|------------------|------------------|------------------|------------------|-----|
| Ser                                  | Leu  | Val              | His              | Ser<br>165      | Asn              | Gly              | Asn              | Thr              | Tyr<br>170       | Leu                | Asn              | Trp              | Tyr              | Leu<br>175       | Gln              |     |
| Lys                                  | Ala  | Gly              | Gln<br>180       | Ser             | Pro              | Lys              | Leu              | Leu<br>185       | Ile              | Tyr                | Lys              | ۷al              | Ser<br>190       | Asn              | Arg              |     |
| Phe                                  | Ser  | Gly<br>195       | ٧a٦              | Pro             | Asp              | Arg              | Phe<br>200       | Ser              | Gly              | Ser                | Gly              | Ser<br>205       | Gly              | Thr              | Asp              |     |
| Phe                                  | Thr<br>210   | Leu              | Lys              | Ile             | Ser              | Arg<br>215       | val              | Gln              | Ala              | Glu                | Asp<br>220       | Leu              | Gly              | Ile              | Tyr              |     |
| Phe<br>225                           | Cys  | Ser              | Gln              | Thr             | Thr<br>230       | His              | val              | Pro              | Pro              | Thr<br>235         | Phe              | Gly              | Gly              | Gly              | Thr<br>240       |     |
| Lys                                  | Leu  | Glu              | Ile              | Lys<br>245      | Arg              | Ser              | Gly              | Gly              | Gly<br>250       | Glу                | Cys              |                  |                  |                  |                  |     |
| <212                                 | <210> 5<br><211> 739<br><212> DNA<br><213> Artificial Sequence |                  |                  |                 |                  |                  |                  |                  |                  |                    |                  |                  |                  |                  |                  |     |
| <220><br><223> 520C9 sFv             |  |                  |                  |                 |                  |                  |                  |                  |                  |                    |                  |                  |                  |                  |                  |     |
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| <400<br>gag<br>Glu<br>1              | atc  | caa              | ttg<br>Leu       | gtg<br>Val<br>5 | cag<br>Gln       | tct<br>Ser       | gga<br>Gly       | cct<br>Pro       | gag<br>Glu<br>10 | ctg<br>Leu         | aag<br>Lys       | aag<br>Lys       | cct<br>Pro       | gga<br>Gly<br>15 | gag<br>Glu       | 48  |
| aca<br>Thr                           | gtc<br>Val   | aag<br>Lys       | atc<br>Ile<br>20 | tcc<br>Ser      | tgc<br>Cys       | aag<br>Lys       | gct<br>Ala       | tct<br>Ser<br>25 | gga<br>Gly       | tat<br>Tyr         | acc<br>Thr       | ttc<br>Phe       | gca<br>Ala<br>30 | aac<br>Asn       | tat<br>Tyr       | 96  |
| gga<br>Gly                           | atg<br>Met   | aac<br>Asn<br>35 | tgg<br>Trp       | atg<br>Met      | aag<br>Lys       | cag<br>Gln       | gct<br>Ala<br>40 | cca<br>Pro       | gga<br>Gly       | aag<br>Lys         | ggt<br>Gly       | tta<br>Leu<br>45 | aag<br>Lys       | tgg<br>Trp       | atg<br>Met       | 144 |
| ggc<br>Gly                           | tgg<br>Trp<br>50   | ata<br>Ile       | aac<br>Asn       | acc<br>Thr      | tac<br>Tyr       | act<br>Thr<br>55 | gga<br>Gly       | cag<br>Gln       | tca<br>Ser       | aca<br>Thr         | tat<br>Tyr<br>60 | gct<br>Ala       | gat<br>Asp       | gac<br>Asp       | ttc<br>Phe       | 192 |
| aag<br>Lys<br>65                     | gaa<br>Glu   | cgg<br>Arg       | ttt<br>Phe       | gcc<br>Ala      | ttc<br>Phe<br>70 | tct<br>Ser       | ttg<br>Leu       | gaa<br>Glu       | acc<br>Thr       | tct<br>Ser<br>75   | gcc<br>Ala       | acc<br>Thr       | act<br>Thr       | gcc<br>Ala       | cat<br>His<br>80 | 240 |
| ttg<br>Leu                           | cag<br>Gln   | atc<br>Ile       | aac<br>Asn       | aac<br>Asn      | ctc<br>Leu       | aga<br>Arg       | aat<br>Asn       | gag<br>Glu       | Asp              | tcg<br>Ser<br>Page | Ala              | aca<br>Thr       | tat<br>Tyr       | ttc<br>Phe       | tgt<br>Cys       | 288 |

| gca<br>Ala        | aga<br>Arg        | cga<br>Arg        | ttt<br>Phe<br>100 | ggg<br>Gly        | ttt<br>Phe        | gct<br>Ala        | tac<br>Tyr        | tgg<br>Trp<br>105 | ggc<br>Gly        | caa<br>Gln        | ggg<br>Gly        | act<br>Thr        | ctg<br>Leu<br>110 | gtc<br>Val        | agt<br>Ser        | 336 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| gtc<br>Val        | tct<br>Ser        | gca<br>Ala<br>115 | tcg<br>Ser        | ata<br>Ile        | tcg<br>Ser        | agc<br>Ser        | tcc<br>Ser<br>120 | tcc<br>Ser        | gga<br>Gly        | tct<br>Ser        | tca<br>Ser        | tct<br>Ser<br>125 | agc<br>Ser        | ggt<br>Gly        | tcc<br>Ser        | 384 |
|                   |                   |                   |                   | tcc<br>Ser        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 432 |
| tct<br>Ser<br>145 | gcc<br>Ala        | tct<br>Ser        | ctg<br>Leu        | gga<br>Gly        | gaa<br>Glu<br>150 | aga<br>Arg        | gtc<br>Val        | agt<br>Ser        | ctc<br>Leu        | act<br>Thr<br>155 | tgt<br>Cys        | cgg<br>Arg        | gca<br>Ala        | agt<br>Ser        | cag<br>Gln<br>160 | 480 |
| gac<br>Asp        | att<br>Ile        | ggt<br>Gly        | aat<br>Asn        | agc<br>Ser<br>165 | tta<br>Leu        | acc<br>Thr        | tgg<br>Trp        | ctt<br>Leu        | cag<br>Gln<br>170 | cag<br>Gln        | gaa<br>Glu        | cca<br>Pro        | gat<br>Asp        | gga<br>Gly<br>175 | act<br>Thr        | 528 |
| att<br>Ile        | aaa<br>Lys        | cgc<br>Arg        | ctg<br>Leu<br>180 | atc<br>Ile        | tac<br>Tyr        | gcc<br>Ala        | aca<br>Thr        | tcc<br>Ser<br>185 | agt<br>Ser        | tta<br>Leu        | gat<br>Asp        | tct<br>Ser        | ggt<br>Gly<br>190 | gtc<br>Val        | ccc<br>Pro        | 576 |
| aaa<br>Lys        | agg<br>Arg        | ttc<br>Phe<br>195 | agt<br>Ser        | ggc<br>Gly        | agt<br>Ser        | cgg<br>Arg        | tct<br>Ser<br>200 | ggg<br>Gly        | tca<br>Ser        | gat<br>Asp        | tat<br>Tyr        | tct<br>Ser<br>205 | ctc<br>Leu        | acc<br>Thr        | atc<br>Ile        | 624 |
| agt<br>Ser        | agc<br>Ser<br>210 | ctt<br>Leu        | gag<br>Glu        | tct<br>Ser        | gaa<br>Glu        | gat<br>Asp<br>215 | ttt<br>Phe        | gta<br>Val        | gtc<br>Val        | tat<br>Tyr        | tac<br>Tyr<br>220 | tgt<br>Cys        | cta<br>Leu        | caa<br>Gln        | tat<br>Tyr        | 672 |
| gct<br>Ala<br>225 | att<br>Ile        | ttt<br>Phe        | ccg<br>Pro        | tac<br>Tyr        | acg<br>Thr<br>230 | ttc<br>Phe        | gga<br>Gly        | ggg<br>Gly        | ggg<br>Gly        | acc<br>Thr<br>235 | aac<br>Asn        | ctg<br>Leu        | gaa<br>Glu        | ata<br>Ile        | aaa<br>Lys<br>240 | 720 |
|                   | gct<br>Ala        |                   | taat              | tctg              | cag               |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 739 |
|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |     |

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Gly Met Asn Trp Met Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met 35 40 \_ 45 Page 7

Gly Trp Ile Asn Thr Tyr Thr Gly Gln Ser Thr Tyr Ala Asp Asp Phe 50 60

Lys Glu Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Thr Thr Ala His 65 70 75 80

Leu Gln Ile Asn Asn Leu Arg Asn Glu Asp Ser Ala Thr Tyr Phe Cys 85 90 95

Ala Arg Arg Phe Gly Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Ser 100 105 110

Val Ser Ala Ser Ile Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser 115 120 125

Ser Ser Ser Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu 130 135 140

Ser Ala Ser Leu Gly Glu Arg Val Ser Leu Thr Cys Arg Ala Ser Gln 145 150 155 160

Asp Ile Gly Asn Ser Leu Thr Trp Leu Gln Gln Glu Pro Asp Gly Thr 165 170 175

Ile Lys Arg Leu Ile Tyr Ala Thr Ser Ser Leu Asp Ser Gly Val Pro 180 185 190

Lys Arg Phe Ser Gly Ser Arg Ser Gly Ser Asp Tyr Ser Leu Thr Ile 195 200 205

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Ser Val Arg Ile Ser Cys Thr Ala Ser Gly Tyr Thr Phe Thr Asn Tyr 20 25 30

Tyr Ile His Trp Leu Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Trp Ile Tyr Pro Gly Asn Gly Asn Thr Lys Tyr Asn Glu Asn Phe 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Phe 65 70 75 80

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Tyr Met Asn Trp Val Arg Gln Ser His Gly Lys Ser Leu Asp Tyr Ile 35 40 45

Gly Tyr Ile Ser Pro Tyr Ser Gly Val Thr Gly Tyr Asn Gln Lys Phe  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95 Page 10

Ala Gly Ser Ser Gly Asn Lys Trp Ala Met Asp Tyr Trp Gly His Gly 100 105 110

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Gly Trp Ile Tyr Pro Gly Asn Gly Asn Thr Lys Tyr Asn Glu Asn Phe 50 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 75 80

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Tyr Ile His Trp Leu Lys Gln Pro Pro Gly Arg Leu Glu Trp Ile Gly 35 40 45

Trp Ile Tyr Pro Gly Asn Gly Asn Thr Lys Tyr Asn Glu Asn Phe Lys 50 60

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Gly Tyr Val Phe Tyr His Gly Thr Ser Asp Asp Thr Thr Pro Leu Arg 50 60

Ser Arg Val Thr Met Leu Val Asp Thr Ser Ser Lys Asn Gln Phe Ser 65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Asn Leu Ile Ala Gly Cys Ile Asp Val Trp Gly Gln Gly Ser 100 105 110

Leu Val Thr Val Ser Ser 115